

What is the relationship between the intake of soy protein and blood lipids among adults without hyperlipidemia?

Conclusion

Moderate evidence suggests soy protein intake may have small effects on total and low-density lipoprotein cholesterol in adults with normal or elevated blood lipids, although results from systematic reviews are inconsistent.

Grade: Moderate

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, [click here](#).

Evidence Summary Overview

This review included four meta-analyses (Harland, 2008; Reynolds, 2006; Weggemans, 2003; Zhan, 2005) and consideration of an additional randomized controlled trial (RCT) (Liao, 2007) and a cross-sectional study (Pan, 2008) that examined the relationship between intake of soy protein and blood lipids among adults without hyperlipidemia published since 2000.

- Harland and colleagues (2008) conducted a meta-analysis of 30 RCTs to determine the effect of a daily intake of circa 25 g (range 10-40g) soy protein on blood lipids in adults with normal or mildly elevated cholesterolemia. They concluded that inclusion of soy protein (circa 25g) resulted in small, significant reductions in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG); no relationship between soy protein and high-density lipoprotein cholesterol (HDL-C) was observed. Reynolds et al, (2006) conducted a meta-analysis of 27 RCTs that examined the effect of isolated soy protein supplementation (20 to >61 grams per day) on serum lipids. Soy protein supplementation reduced TC, LDL-C and TG and increased HDL-C among adults with and without hypercholesterolemia. Zhan et al, (2005) conducted a meta-analysis with 23 RCTs to identify the effects of soy protein containing isoflavones on lipid profile. They concluded that soy protein containing isoflavones significantly reduced serum TC, LDL-C and TG and significantly increased HDL-C; however, greater reductions of TC were seen among participants with hypercholesterolemia than those without, and no significant effect on HDL-C was observed among participants with normal initial lipid levels. Weggemans and colleagues (2003) examined the effect of soy protein (19-60 g per day) with isoflavones on cholesterol concentrations in trials substituting soy protein with dairy or other animal protein sources. The authors concluded that changes in soy protein amount are not related to decreases in LDL-C or increases in HDL-C
- There was considerable overlap among the studies considered in the four reviews. The number of articles unique to each review were 17 of 30 for Harland et al, (2008), 11 of 27 for Reynolds et al, (2006), nine of 23 for Zhan et al, (2005), and one of 10 for Weggemans et al, (2003). Four studies were included in all four of the meta-analyses. Differences in articles included in these reviews can be partially explained by inclusion criteria; for example, Weggemans et al, (2003) only included trials that substituted soy protein with dairy or other animal protein

sources, while the other reviews also considered control groups consuming other protein sources (e.g., casein or whey)

- Two additional primary citations were identified in the Nutrition Evidence Library (NEL) review that were not captured in any of the meta-analyses. Liao and colleagues (2007) conducted an RCT with isocaloric diets providing 1,200kcal per day from either soy protein or animal and plant protein for eight weeks. They reported greater decreases in TC and LDL-C among participants receiving soy protein than the control group but no changes in TG or HDL-C were observed in either group. In a cross-sectional study, Pan et al, (2008) reported that there were no significant (NS) relationships between soy protein and hypertriglyceridemia or low HDL-C. The median level of soy protein intake was 7.8g per day.

Evidence Summary Paragraphs

Systematic Reviews

Harland et al, 2008 (positive quality), a systematic review, meta-analysis and regression of RCTs, determined the effect of a daily intake of circa 25g soy protein on blood lipids in adults with normal or mildly elevated cholesterolemia. Randomized controlled trials published from January 1995 to September 2007 were identified by searching Medline with additional searches in Embase, SciSearch and Current Contents as well as hand searches and review of reference lists. Search terms used were “SOY(A)” and “CHOLESTEROL or BLOOD LIPIDS”. A total of 172 RCTs were identified in searches. Inclusion criteria for the review were:

1. An original RCT, parallel or crossover design, published in a peer-reviewed journal and included a suitable (non-soy protein) control treatment
2. Soy protein intake was CA 25g (range 10-40g) and could be derived from ISP, soy protein concentrates or soy foods
3. Volunteers were healthy or mild hypercholesterolemic, with weight loss less than 2kg per day and average BMI<30kg/m²
4. Study duration was a minimum of four weeks or one menstrual cycle. Thirty RCTs containing 42 treatment arms (N=2,913 adults) were included in analyses.

Average soy protein intake in the 30 studies was 26.9g (range 15-40g); study duration was from four to 52 weeks; study population average age range was 27-67 years. The main source of soy protein was ISP (17 studies), and in the remaining studies soy foods either of a traditional nature or prepared specifically for the study were used (13 studies). Soy protein inclusion led to reductions in standard difference in mean LDL, TC and blood TG of 0.23mmol/L (95% CI: -0.160, -0.306, P<0.0001), 0.22mmol/L (95% CI: -0.142, -0.291, P<0.0001) and 0.08mmol/L (95% CI: -0.004, -0.158; P=0.04), respectively. There was increase in HDL-C of 0.071mmol/L (95% CI: -0.002, 0.144), which did not reach significance (P=0.057). Meta-regression analysis indicated no dose response relationship between soy protein intake in the range of 15-40g and standard difference in LDL or HDL. The authors concluded that the inclusion of soy protein (circa 25g) into the diet of adults with normal or mild hypercholesterolemia resulted in small, significant reductions in TC and LDL-C and TGs. (Note: Authors from HarlandHall Associates and Nutrilicious.)

Reynolds et al, 2006 (positive quality) examined the effect of soy protein supplementation on serum lipid levels by pooling the results from RCTs of isolated soy protein supplementation. English language articles were retrieved by searching MEDLINE (1966 to February 2005) using the following medical subject headings: Lipids, lipoproteins, LDL-C, HDL-C, VLDL-C, cholesterol, soybean proteins and soybeans. Bibliographies of the retrieved articles were also reviewed. 147 studies were reviewed for inclusion. Each study had to have been a RCT; been conducted in adults; used concurrent control groups; have limited intervention differences between groups to soy protein

supplementation in the form of isolated soy protein; and reported changes in serum lipids (TG, TC, LDL-C or HDL-C) from baseline to follow-up and the corresponding variances or sufficient data to estimate them. 27 reports (totaling 41 comparisons; N=1,756 adults) were included in analyses. Soy intake ranged from 20 to >61g per day, and isoflavone intake ranged from 2 to 192mg per day. Mean age range was 22-67 years and duration of intervention ranged from 3 to 52 weeks. Of the 31 trials that reported on the hypercholesterolemic status, 19 were conducted in participants with hyperlipidemia (as defined by the study), nine were conducted in participants with normal lipid levels and three trials included participants with and without hyperlipidemia. Soy protein supplementation was associated with a significant reduction in mean serum TC (-5.26mg/dL, 95% CI: -7.14, -3.38; P<0.0001), LDL-C (-4.25mg/dL; 95% CI: -6.00, -2.50; P<0.0001) and TG (-6.26mg/dL, 95% CI: -9.14, -3.38; P<0.0001) and a significant increase in HDL-C (0.77mg/dL, 95% CI: 0.20, 1.34; P=0.008). Soy protein supplementation reduced total and LDL-C levels consistently in all subgroups. However, the effect size of soy protein supplementation on TC and LDL-C was slightly greater in participants with a mean baseline TC level of <240mg/dL and LDL-C level of <160mg/dL compared with those with elevated cholesterol levels (TC ≥240mg/dL or LDL-C ≥160mg/dL) and among pre- or peri-menopausal women compared with post-menopausal women. In contrast, the effect of soy protein supplementation on HDL-C was slightly greater in participants with elevated TC levels at baseline (TC ≥240mg/dL) compared with participants with TC levels <240mg/dL. Meta-regression analyses showed a dose-response relation between soy protein and isoflavone supplementation and net changes in serum lipids. The authors concluded that soy protein supplementation reduces serum lipids among adults with or without hypercholesterolemia and replacing foods high in saturated fat, trans-saturated fat, and cholesterol with soy protein may have a beneficial effect on coronary risk factors. (Note: Partially supported by grant from NIH.)

Zhan et al, 2005 (neutral quality) conducted a meta-analysis to identify and quantify the effects of soy protein containing isoflavones on the lipid profile. Randomized controlled trials published from 1995 to 2002 were identified from PUBMED and examination of cited references. Forty-six studies were reviewed for inclusion. Studies were selected for analysis if they met the following criteria:

1. They provided the amount of soy isoflavones
2. They were controlled and had either a randomized crossover or a parallel design
3. They provided initial lipid profile concentrations.

Further, studies were excluded if whole soybean rather than soy protein was used. Twenty-three studies (providing 52 comparisons; N=1,381 adults) were included in analyses. In nine studies with 27 comparisons, the subjects had hypercholesterolemia at baseline according to the definitions of the original study. Sixteen studies used isolated soy protein containing isoflavones, three used tablets containing extracted isoflavones and three used textured soy food. Isoflavone concentrations contained in soy protein averaged 80mg per day. The trials varied in length from three to 26 weeks. Most control groups received casein or whey; the control group received meat or milk in three trials. Soy protein with isoflavones intact was associated with significant decreases in serum TC (by 0.22mmol/L, or 3.77%), LDL-C (by 0.21mmol/L, or 5.25%), and TG (by 0.10mmol/L, or 7.27%) and significant increases in serum HDL-C (by 0.04mmol/L or 3.03%). Subjects with hypercholesterolemia had greater reductions of TC than did normal subjects. The TC concentrations of the former decreased by 0.25mmol/L (95% CI: -0.33, -0.17; P<0.0001) and those of the latter decreased by 0.17mmol/L (95% CI: -0.25, -0.08; P<0.0001). Initial lipid concentrations did not influence changes in LDL-C or TG; those with normal and high initial lipids levels had similar, significant net changes. However, soy protein containing isoflavones had a significant effect on HDL-C among subjects with hypercholesterolemia (net change = 0.10mmol/L; 95% CI: 0.06, 0.13; P<0.0001), but no significant effect on HDL-C was observed among participants with normal initial

lipid levels. The authors concluded that soy protein containing isoflavones significantly reduced serum TC, LDL-C and TG, and significantly increased HDL-C and changes were related to initial serum lipid concentrations of the subjects. (Note: Supported by the Centre of Research and Promotion of Women's Health.)

Weggemans et al, 2003 (positive quality) examined the effect of soy-associated isoflavones on cholesterol concentrations in trials substituting soy protein with dairy or animal protein. Studies were identified by MEDLINE searches (1995 to June 2002) and reviewing reference lists. Search terms were soy OR isoflavones AND cholesterol. One hundred forty eight studies were reviewed for inclusion. Inclusion criteria included: Composition of the experimental diets differed only in the amount of soy and animal proteins and in the amount of soy-associated isoflavones; participants were weight stable; minimum two weeks feeding trial; and parallel or Latin Square crossover design. Ten studies (providing 21 comparisons; N=959 adults) were included in analyses. The intake of soy-associated isoflavones increased by one-95 mg per day, and the intake of soy protein increased by 19-60g per day. During the soy treatment period, subjects were provided with isolated soy protein, a soy protein supplement, textured soy protein or tofu. During the control treatment period, casein, dry milk, a milk protein supplement, dairy and egg protein or cooked lean meat were given, if necessary, in combination with other foods to balance the change in macronutrient intake. Average age ranged from 41-67 years, and baseline cholesterol concentration ranged from 5.42 to 6.60 mmol/L. Feeding daily 36g soy protein with 52mg soy-associated isoflavones on average decreased LDL-C by -0.17 ± 0.04 mmol/L (mean \pm SE) and increased HDL-C by 0.03 ± 0.01 mmol/L. There was no dose-response relation between soy-associated isoflavones and changes in LDL-C ($R = -0.33$, $P = 0.14$) (Pearson correlation coefficient) or HDL-C ($R = -0.07$, $P = 0.76$) or their ratio. Correlations between changes in soy protein and blood cholesterol and lipoprotein concentrations were also not significant. No significant effect of baseline cholesterol on cholesterol lowering was observed; the authors noted the small range in baseline cholesterol values. Replacing dairy and animal proteins with soy protein led to 4% lower LDL-C concentrations and significantly increased HDL-C concentrations by 3%. The authors concluded that changes in soy-associated isoflavones or in soy protein amount are not related to decreases in LDL or increases in HDL-C. (Note: Sponsored by Unilever Research and Development.)




Primary Citations




Liao et al, 2007 (positive quality), an RCT, examined the effects of a soy-based diet compared with a traditional low-calorie diet on weight loss and blood lipid levels in 30 obese adults (mean BMI $29-30 \text{ kg/m}^2$; 80% female) in China. Participants were randomized to two groups: The soy-based low-calorie group consumed soy protein as the only protein source, and the traditional low-calorie group consumed two-thirds animal protein and the rest plant protein in a 1,200kcal per day diet for eight weeks. Anthropometric data were acquired every week, and biochemical data from before and after the eight-week experiment were compared. Body weight, BMI, body fat percentage and waist circumference significantly decreased in both groups (all $P < 0.05$), but there were no differences between groups. Serum TC concentrations and LDL-C concentrations decreased in the soy-based group and were significantly different from measurements in the traditional group ($P < 0.05$ for both). The changes in TC for the soy and traditional groups were -23.7 ± 15.7 and -18 ± 18.0 mg/dL, respectively, and the changes in LDL-C were -15.4 ± 7.7 and -9.0 ± 16.5 mg/dL, respectively. No significant change in serum TG levels or serum HDL-C levels was found in the soy or traditional group. The authors concluded that a weight-loss diet containing high-quality soy products as the main source of protein could improve hyperlipidemia associated with obesity during a weight-loss program.

Pan et al, 2008 (neutral quality) evaluated the association between soy protein intake and the risk of

MetS and its components (including hypertriglyceridemia and low HDL-C) in a cross-sectional analysis of 2,811 adults (58% female; age 58.4+6.0 years) from the Nutrition and Health of Aging Population Project in China. Blood samples were collected during physical examinations at local health stations or community clinics. Data on nutrient intake in the year prior to enrollment were derived from a quantitative FFQ that was administered during a personal interview. The FFQ included 74 food items and groups. Seven soy food items responsible for the majority of soy consumption were listed within the questionnaire, including fresh and dried soybeans, tofu, soy milk, jelly bean curd, soy sauce and other processed soy products. In the total sample, soy protein intake was not associated with hypertriglyceridemia (P=0.749) or low HDL-C (P=0.906); similarly, no significant relationships were observed when men and women were analyzed separately.

 [View table in new window](#)


Author, Year, Study Design, Class, Rating	Study Description/Location	Soy Protein Association (Pos, Neg, None)
Harland et al. 2008 Study Design: Meta-analysis : Systematic Review Class: M Rating: 	30 studies.	Soy protein (circa 25g, range 10 to 40g): (-) TC, (-) LDL-C, (-) TG, Ø HDL.
Liao et al 2007 Study Design: randomized intervention trial Class: A Rating: 	Location: China.	Weight loss diet with soy protein: (-) TC, (-) LDL-C, Ø TG, Ø HDL-C.
Pan et al 2008 Study Design: cross sectional study Class: D Rating: 	Nutrition and Health of Aging Population Project. Location: China.	Soy protein intake: Ø hypertriglyceridemia, Ø low HDL-C.


Reynolds et al. 2006 Study Design: Meta-analysis Class: M Rating: 	27 studies.	Isolated soy protein supplementation (20 to >61g per day): (-) TC, (-) LDL-C, (-) TG, (+) HDL.
Weggemans RM and Trautwein EA, 2003 Study Design: Meta-analysis Class: M Rating: 	10 studies.	Soy protein (19-60g per day) with isoflavones compared to dairy or other animal protein sources: Ø LDL-C, Ø HDL-C.
Zhan and Ho 2005 Study Design: Meta-analysis Class: M Rating: 	23 studies.	Soy protein with isoflavones: (-) TC, (-) LDL-C, (-) TG, Ø HDL-C.


Research Design and Implementation Rating Summary

For a summary of the Research Design and Implementation Rating results, [click here](#).


Worksheets


 [Harland JJ, Haffner TA. Systematic review, meta-analysis and regression of randomised controlled trials reporting an association between an intake of circa 25 g soya protein per day and blood cholesterol. Atherosclerosis. 2008;200\(1\):13-27](#)

 [Liao FH, Shieh MJ, Yang SC, Lin SH, Chien YW. Effectiveness of a soy-based compared with a traditional low-calorie diet on weight loss and lipid levels in overweight adults. Nutrition. 2007 Jul-Aug;23\(7-8\):551-6](#)

 [Pan A, Franco OH, Ye J, Demark-Wahnefried W, Ye X, Yu Z, Li H, Lin X. Soy protein intake has sex-specific effects on the risk of metabolic syndrome in middle-aged and elderly Chinese. J Nutr. 2008 Dec;138\(12\):2413-21.](#)

 [Reynolds K, Chin A, Lees KA, Nguyen A, Bujnowski D, He J. A meta-analysis of the effect of soy protein supplementation on serum lipids. Am J Cardiol. 2006;98\(5\):633-40](#)

 [Weggemans RM, Trautwein EA. Relation between soy-associated isoflavones and LDL and HDL cholesterol concentrations in humans: a meta-analysis. *European Journal of Clinical Nutrition* 2003. 57: 940-994.](#)

 [Zhan, Siyan and Suzzanne C Ho Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile Am J Clin Nutr 2005;81:397-408](#)